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## **CLAIMS**

We claim:

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1. A humanized CC49 antibody, comprising a non-conservative amino acid substitution in a light chain complementarity determining region 3 of the CC49 antibody, or functional fragment of the humanized CC49 antibody, that has a high binding affinity for TAG-72.

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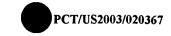
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- 2. The antibody of claim 1, wherein the non-conservative substitution is a tyrosine to proline substitution.
- 3. The antibody of claim 1, wherein the non-conservative substitution is at position 91.
  - 4. The antibody of claim 1, wherein the non-conservative substitution is at a residue that is a ligand contact residue.
- 5. The antibody of claim 1, wherein the functional fragment is an Fab fragment, an Fv fragment, or an F(ab')<sub>2</sub> fragment.
  - 6. The antibody of claim 1, wherein a light chain complementarity determining region 1 and a light chain complementarity determining region 2 are from a human antibody.
  - 7. The antibody of claim 1, wherein the light chain complementarity determining region 3, a heavy chain complementarity determining region 1, a heavy chain

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complementarity determining region 2, and a heavy chain complementarity determining region 3 are from a murine CC49 antibody.

- 8. The antibody of claim 1, wherein the high binding affinity is at least about  $1.2 \times 10^{-8} M$ .
  - 9. The antibody of claim 8, wherein the high binding affinity is at least about  $1.5 \times 10^{-8}$ , about  $2.0 \times 10^{-8}$ , about  $2.5 \times 10^{-8}$ , about  $3.0 \times 10^{-8}$ , about  $3.5 \times 10^{-8}$ , about  $4.5 \times 10^{-8}$ , or about  $5.0 \times 10^{-8}$  M.
  - 10. The antibody of claim 1, wherein the antibody is minimally immunogenic.
  - 11. The antibody of claim 1, wherein the antibody further comprises an effector molecule.
  - 12. The antibody of claim 11, wherein the effector molecule is a detectable label.
  - 13. The antibody of claim 12, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.
  - 14. The antibody of claim 11, wherein the effector molecule is a toxin.
- 15. The antibody of claim 14, wherein the toxin is a chemotherapeutic drug, aradioactive isotope, a bacterial toxin, a viral toxin, a cytokine or a venom protein.
  - 16. The antibody of claim 1, further comprising at least one additional non-conservative amino acid substitution in a light chain complementarity determining region.

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- 17. The antibody of claim 16, wherein the light chain complementarity determining region is a light chain complementarity determining region 1, a light chain complementarity determining region 2, or a light chain complementarity determining region 3.
- 18. The antibody of claim 1, further comprising at least one non-conservative amino acid substitution in a heavy chain complementarity determining region.
- 19. The antibody of claim 18, wherein the heavy chain complementarity determining region is a heavy chain complementarity determining region 1, a heavy chain complementarity determining region 2, or a heavy chain complementarity determining region 3.
- 15 20. A humanized CC49 antibody, wherein a nucleic acid sequence encoding the antibody has an ATCC Accession number comprising ATCC Accession number PTA-4182 or ATCC Accession number PTA-4183.
- 21. A nucleic acid molecule encoding the humanized monoclonal antibody of 20 claim 1.
  - 22. A vector comprising the nucleic acid of claim 21.
  - 23. A humanized CC49 antibody, comprising:
- a variable light framework region and a variable heavy framework region of a human antibody;
  - a complementarity determining region, wherein at least one complementarity determining region is from the human antibody and the remaining complementarity determining regions are from a murine CC49 antibody;



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a non-conservative substitution of a first residue in a light chain complementarity determining region 3; and

a substitution of a second residue in a complementarity determining region of the human CC49 antibody;

- wherein the humanized CC49 antibody has a high binding affinity for TAG-72 and is minimally immunogenic.
  - 24. The antibody of claim 23, wherein the non-conservative substitution is a tyrosine to proline substitution.
  - 25. The antibody of claim 23, wherein the non-conservative substitution is at position 91.
- 26. The antibody of claim 25, wherein the non-conservative substitution at position91 is a tyrosine to proline substitution.
  - 27. The antibody of claim 23, wherein the antibody further comprises an effector molecule.
- 20 28. The antibody of claim 27, wherein the effector molecule is a detectable label.
  - 29. The antibody of claim 28, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.
  - 30. The antibody of claim 27, wherein the effector molecule is a toxin.
  - 31. The antibody of claim 30, wherein the toxin is a chemotherapeutic drug, a radioactive isotope, a bacterial toxin, a viral toxin, a cytokine or a venom protein.

- 32. A method of detecting a TAG-72-expressing tumor in a subject, comprising:

  contacting a sample obtained from the subject with the antibody of claim

  1 for a sufficient amount of time to form an immune complex;
- detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.
- 33. The method of claim 32, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.
  - 34. The method of claim 32, wherein the antibody further comprises an effector molecule.
- 15 35. The method of claim 34, wherein the effector molecule is a detectable label.
  - 36. The method of claim 35, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.

37. The method of claim 32, further comprising contacting the antibody with a secondary antibody.

- 38. The method of claim 37, wherein the secondary antibody further comprises a detectable label.
  - 39. A method of detecting a TAG-72-expressing tumor in a subject, comprising: administering the antibody of claim 1 to the subject for a sufficient amount of time to form an immune complex;

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detecting the presence of the immune complex, wherein the presence of the immune complex demonstrates the presence of the TAG-72-expressing tumor.

- 40. The method of claim 39, wherein the antibody further comprises an effector molecule.
  - 41. The method of claim 40, wherein the effector molecule is a detectable label.
- 42. The method of claim 41, wherein the detectable label comprises a radioactive isotope, an enzyme substrate, a co-factor, a ligand, a chemiluminescent agent, a fluorescent agent, a hapten, or an enzyme.
- 43. The method of claim 39, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.
  - 44. A method of treating a subject having a tumor that expresses TAG-72, comprising administering to the subject a therapeutically effective amount of the antibody of claim 1, wherein administering the therapeutically effective amount of the antibody of claim 1 inhibits the growth of the tumor or reduces the size of the tumor, thereby treating the subject.
    - 45. The method of claim 44, wherein the administration of a therapeutically effective amount of the antibody of claim 1 does not elicit a human anti-murine antibody response in a subject.
    - 46. The method of claim 44, wherein the tumor is a colorectal tumor, a gastric tumor, a pancreatic tumor, a breast tumor, a lung tumor, an adenocarcinoma, or an ovarian tumor.

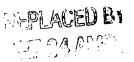
- 47. The method of claim 44, wherein the antibody further comprises an effector molecule.
- 5 48. The method of claim 47, wherein the effector molecule is a toxin.
  - 49. The method of claim 48, wherein the toxin is a chemotherapeutic drug, a radioactive isotope, a bacterial toxin, a viral toxin, a cytokine, or a venom protein.
- 10 50. The method of claim 49, wherein the antibody comprising a radioactive isotope is used in radioimmunotherapy.
  - 51. A method of treating a subject having a tumor that expresses TAG-72, comprising:
- administering the antibody of claim 1 to the subject for a sufficient amount of time to form an immune complex, wherein the antibody comprises a radioactive isotope;

detecting the presence of the immune complex with a hand-held gamma counter, wherein the presence of the immune complex demonstrates the presence of the

- 20 TAG-72-expressing tumor; and
  - removing the tumor surgically, thereby treating the subject.
  - 52. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of claim 1 in a pharmaceutically acceptable carrier.

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53. A kit, comprising a container comprising the antibody of claim 1.



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54. The kit of claim 53, further comprising a container containing an antigen, a container containing a secondary antibody conjugated to a chemical compound, instructions for using the kit, or any combination thereof.